eSupplement 2: Aerobic Interval Training

Background
Various mechanisms have been proposed that may explain the effectiveness of aerobic training in individuals with MS, including improvements in fitness-related parameters, normalization of hormonal function (in particular the hypothalamic–pituitary–adrenal axis), and changes in neuroinflammatory and neuro-protective biomarkers. Positive effects of exercise therapy, and aerobic training in particular, have been shown for outcomes on all levels of the International Classification of Functioning (ICF) model.

Equipment
Aerobic interval training was performed on a Kettler X7 hometrainer situated at the study centre. In addition, participants were provided with identical exercise equipment at their home for the duration of the intervention period of 16 weeks. Heart rate was monitored and a BORG scale (6-20) was used to assess perceived exertion. Participants were provided with a log (see Table 1) in which training intensity and each training session was recorded.

Table 1. Example of a training week in the participants' log

WEEK: example								
Day	**Date**	**Time of day**			**Finished?**	**N minutes**	**BORG**	**If terminated early, provide reason:**
		9-12am	12am – 6pm	6-10pm				
Monday					YES/NO			
Tuesday		x			YES/~~NO~~	30	14	
Wednesday					YES/NO			
Thursday			x		YES/~~NO~~	30	15	
Friday					YES/NO			
Saturday					YES/NO			
Sunday				x	~~YES~~/NO	16	18	Extremely tired
Notes: - Had the flu last week - …..								

Provider
Trained physiotherapist experienced in treating MS patients.

Supervision
Of a total of 48 prescribed individual sessions, 12 sessions took place in the outpatient clinic and were supervised by the physiotherapist. During the first two weeks of training, two out of three sessions a week were supervised, and one was home-based. Over the following 6 weeks, one session a week was supervised and two were home-based. During the final 8 weeks, 1 session every two weeks was supervised while the remainder were home-based.

Duration and frequency
Aerobic training lasted 16 weeks, with a frequency of 3 times a week. Participants were advised to take at least one rest-day between sessions. However, participants were free to schedule home-based sessions in line with their own agenda. Each session had a duration of 30 minutes, excluding short warming-up and cooling-down periods, and consisted of 6 cycles of interval training with the first 3 minutes at 40% peak power, 1 minute at 60% peak power and 1 minute at 80% peak power (see figure 1).

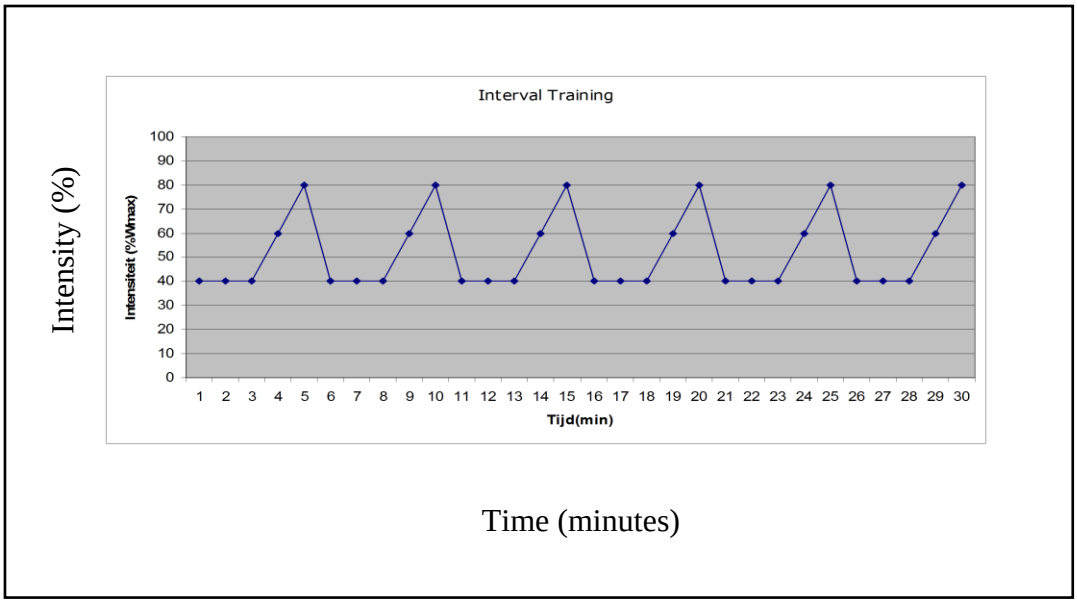

Figure 1. Schematic view of one aerobic training session (30 minutes)

Intensity

Both prior to and half-way through (8 weeks) the aerobic training period of 16 weeks, participants underwent a maximal cardiopulmonary exercise test, which included gas-exchange measurements to assess peak oxygen uptake and peak power. For the purpose of the TREFAMS-AT trial, exercise intensity was based on the percentage of peak power. Using this approach, we could be certain that 1) the protocolled intensity would be within the scope of what was feasible for that specific subject (opposed to, for instance, using a Astrand submaximal exercise test), and 2) we could derive a very specific measure of adherence by calculating the protocolled workload versus the achieved workload. Exercise intensities were adjusted based on the exercise test at 8 weeks so as to ensure that in the case of a lower outcome, exercise intensities were maintained, and in case of a higher outcome, intensities could be adjusted in line with the new peak power output.

Modifications

In some cases, participants had an exceptionally good or bad day during the exercise test and may therefore have been allocated too heavy or too light training intensities. Whether this was the case was determined by the supervising physiotherapist, together with the participant. Exercise intensity was then adjusted accordingly in the following manner:

1) the actual workload was reduced by a maximum of 20% such that the original intensity for the 4th minute now represented a peak intensity of 80%.
2) if this was still too demanding, the number of cycles was reduced by a maximum of two.
3) if the above was still insufficient, the middle training session was made optional to allow participants a longer period of rest between sessions.

Adherence

A gradual reduction in supervision was based on the hypothesis that greater early stage supervision was required to allow fine-tuning of the training regime, and to allow feedback to be provided in response to questions related to training, experience of symptoms, or other possible issues. As participants gained familiarity with the training protocol, supervision would be reduced. During the final 8 weeks, supervision was reduced further in order to address the self-supporting capacity of the participants. In addition, by using peak power as a means to describe exercise intensity we could derive measures of adherence including:

1) the number of sessions started or completed versus the number of sessions prescribed.
2) the actual work load (Watt) versus the prescribed work load.